REMARKS

Claims 1-25 are pending in this application. By this amendment, Claim 24 has been amended. No new matter has been added thereby. The amendment to Claim 24 should be entered because it complies with the Examiner's suggestion that the claim should contain further limitations directed to the evaporation of the solvent. Accordingly, no showing under 37 CFR 1.116(b)(3) should be required. The Examiner's rejections are traversed below.

Claim Rejection Under 35 U.S.C. § 102

Applicant notes that the Examiner has withdrawn the previous rejection of Claims 1-9 and 11-25 under 35 U.S.C. § 102(b) as anticipated by Golz-Berner et al., PCT Publication No. WO 99/66881 (using U.S. Patent No. 6,426,080 as an English equivalent).

The Examiner has rejected Claims 1-2, 6-10, 12-18, and 20-25 under 35 U.S.C. § 102(b) as anticipated by Mitchell et al., U.S. Patent No. 5,462,946 and for the reasons set forth in the previous Office Action mailed April 11, 2006. Applicant notes that Claim 18 was canceled in the previous Amendment and Response filed August 15, 2006. Applicant traverses these rejections with respect to Claims 1-2, 6-10, 12-17, and 20-25.

The Examiner states that Mitchell discloses "the use of the pharmaceutical composition as an ointment, cream or lotion and an aerosol drop or spray which would satisfy the limitation of a low residue gel or low residue thickened liquid." The Examiner is incorrect; Mitchell does not disclose a topical formulation that satisfies either the "low-residue gel" or "low-residue thickened liquid" limitations of the pending claims.

As noted in Applicant's previous Response, the use of an ointment, cream or lotion form of a radioprotective composition shortly before the administration of radiation leaves a residue or film that leads to potentially severe topical burning. *See* specification at pp. 2, 15. This is clear from standard definitions of these terms. According to the U.S. Food and Drug Administration's Center for Drug Evaluation and Research Data Standards Manual[1], for example, an "ointment" is "[a] semisolid dosage form, usually containing <20% water and volatiles and >50% hydrocarbons, waxes, or polyols as the vehicle." Furthermore, a "cream" is "an emulsion, semisolid dosage form, usually containing > 20% water and volatiles and/or < 50% hydrocarbons, waxes, or polyols as the vehicle." Dosage forms containing such significant

[1] Available at http://www.fda.gov/cder/dsm/DRG/drg00201.htm.

amounts of residue-producing substances will not be "low-residue." Neither are "lotions" limited to low-residue forms: they are defined simply as "[a]n emulsion, liquid dosage form." Indeed, guidelines to patients undergoing radiation therapy generally counsel specifically against the use of lotions on the treated area during therapy.[2]

Nor does Mitchell disclose topical ionizing radiation protectant formulations in the form of aerosols, drops, or sprays. These forms are listed in other contexts, such as protectant compositions for use against eye diseases or as therapy for humans or plants exposed to paraquat. Even if such forms were employed as topical radiation protectant formulations, which is neither disclosed in nor suggested by Mitchell, Mitchell does not disclose that such formulations should be low-residue formulations.

Mitchell simply does not disclose "low-residue" liquids or gels. Although the relevance of this gap in the Mitchell disclosure may be "unclear" to the Examiner[3], it represents a clear legal deficiency in the pending anticipation rejection. It is black letter law that to anticipate a claim, the cited reference must teach every limitation of the rejected claims.[4] "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Because Mitchell does not disclose the "low-residue gel" or "low-residue thickened liquid" limitations of Claims 1, 13, 15, 16, and 25, the rejection of those claims on this ground is improper and Applicant requests that it be withdrawn.

Claim 24 has been amended to require that "sufficient solvent [be evaporated] to substantially reduce topical burning on application of radiotherapy." Support for this amendment may be found, for example, at page 14, lines 21-27 of the specification. As recognized by the

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[2] See, for example, the American Cancer Society's Detailed Guide: Breast Cancer: Radiation Therapy (available at http://www.cancer.org/docroot/CRI/content/CRI_2_4_4X_Radiation_Therapy_5.asp?sitearea=CRI&viewmode=print&) ("Lotions, powders, deodorants, and antiperspirants can interfere with external beam radiation therapy, so you should avoid using them until treatments are complete."); University of Texas MD Anderson Cancer Center, Radiotherapy: Frequently Asked Questions (available at http://www.mdanderson.org/care_centers/radiationonco/dindex.cfm?pn=D1765CAF-8E4C-11D4-80FA00508B603A14#q14) ("Do not put anything (cream, lotion, powder, makeup) on the treatment area unless your doctor or nurse says it is OK.").

[3] See Office Action mailed September 15, 2006 at 2.

[4] See M.P.E.P. § 2131.

Examiner, Mitchell is silent as to the specific solvents to be employed. *See* Office Action mailed April 11, 2006 at page 2. Mitchell does not disclose that enough of the undisclosed solvent in the "ointment, lotion, or cream" formulation will evaporate before ionizing radiation is applied to substantially reduce topical burning. Nor is such evaporation of the solvent inherent in Mitchell. "Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999); *see also* M.P.E.P. § 2112(IV). Rather, "the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference." *In re Robertson*, 169 F.3d at 745. A disclosure of sufficient evaporation of the solvent before the application of ionizing radiation to avoid radiation-associated topical burning is not "necessarily present" in Mitchell. *Id.* For this reason, the Mitchell disclosure does not literally or inherently anticipate Claim 24, and Applicant requests that this rejection be withdrawn.

The remaining claims rejected over Mitchell depend from one of the independent claims described above, and contain all the limitations thereof. Because Mitchell does not anticipate the pending independent claims as amended, it cannot anticipate the claims depending from these independent claims.

Thus, none of Claims 1-2, 6-10, 12-17, and 20-25 are anticipated by Mitchell. Applicant requests that this rejection be withdrawn.

Claim Rejection Under 35 U.S.C. § 103

The Examiner has rejected Claims 1-25 under 35 U.S.C. § 103(a) as being unpatentable over Mitchell et al., U.S. Patent No. 5,462,946, in view of Golz-Berner et al., PCT Publication No. WO 99/66881. Claim 18 was canceled in the Response filed on August 15, 2006. Applicant traverses this rejection with respect to Claims 1-17 and 19-25.

The topical formulations of the present application are designed to leave little residue on the skin after a short period of time, in order to ameliorate or avoid the problem of burning caused by radiotherapy. Neither Mitchell nor Golz-Berner disclose or suggest a low-residue formulation such as that presently claimed.

As noted above, Mitchell discloses the use of a radioprotective formulation in the form of an ointment, cream, or lotion. None of these formulations satisfy the "low-residue" limitation of the claims.

The Examiner relies on Golz-Berner for "its disclosure of cosmetic active substances to protect the skin and the use of solvents, carriers, and hydrogels." When Golz-Berner is considered in its entirety, as is required, see M.P.E.P. §2141.02(VI), its disclosure would not lead one of skill in the art to a low-residue gel or low-residue thickened liquid, as the Examiner states.

Golz-Berner is concerned with the preparation of cosmetic preparations, with one stated objective of the invention being "to provide a preparation of active substances that keeps its radical protection potential over a long period of time." Golz-Berner at col. 1, lines 52-54. In its broadest disclosure, Golz-Berner teaches that the preparation achieves an incorporation of the active ingredients in an "association complex" containing not only the hydrogel components identified by the Examiner, but also a significant fraction of phospholipids (up to 30% by weight). *See* Golz-Berner at col. 2, lines 11-12; col. 3, lines 37-42. One of skill in the art, on reviewing the Golz-Berner reference for disclosure of how to prepare a topical radioprotective formulation, would also incorporate these phospholipids into the formulation to form a similar association complex with the nitroxide active ingredient. The phospholipids, which have a much higher molecular weight than the disclosed solvents, would not readily evaporate, and the resulting composition would leave a residue that would cause topical burning during radiotherapy.

Furthermore, although the Examiner has treated the examples of Golz-Berner as non-limiting, those examples must be considered for what they would suggest to one of skill in the art. See *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983). As noted in the previous Response, Golz-Berner discloses exemplary cosmetic compositions, some of which are described as "creams." This term coincides with Mitchell's teaching that a "cream" form should be used for the radioprotective formulation, making it more likely that one of skill would follow the specific teachings disclosed. Each of these exemplary "cream" formulations contains not only the phospholipid-containing active complex, but also a considerable amount of glycerine, as previously noted. *See* Response filed August 15, 2006 at 9. Glycerine is highly hygroscopic and will slow the rate of evaporation of the solvents employed in the compositions. Because a

significant amount of not only phospholipid but also glycerine is included in each of the exemplary "creams" disclosed in Golz-Berner, topical formulations made following the teachings of Golz-Berner would not result in the "low-residue gels" or "low-residue thickened liquids" required by Claims 1, 13, 15, 16, and 25. Neither, given the presence of these ingredients, would the resulting formulations meet the requirements of amended Claim 24, wherein evaporation of sufficient solvent to substantially reduce the burning effect occurs before radiotherapy is applied.

As a result, even if the teachings of Golz-Berner were combined with those of Mitchell, a "low-residue" gel or thickened liquid would not result. Because this limitation, and the limitation of Claim 24 discussed above, are not found in the cited prior art references, a prima facie case of obviousness has not been established. Claims 1-17 and 19-25, as presently amended, are not obvious over the cited prior art, and withdrawal of this rejection is respectfully requested.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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